

CLAIMS:

1. A method of modulating one or more mammalian endothelial cell functional characteristics, said method comprising modulating the functional level of sphingosine kinase wherein inducing over-expression of said sphingosine kinase level modulates one or more of the functional characteristics of said endothelial cell.
2. A method of modulating one or more endothelial cell functional characteristics in a mammal, said method comprising modulating the functional level of sphingosine kinase wherein inducing over-expression of said sphingosine kinase level modulates one or more of the functional characteristics of said endothelial cell.
3. A method for the treatment and/or prophylaxis of a condition characterised by aberrant or otherwise unwanted endothelial cell functioning in a mammal, said method comprising modulating the functional level of sphingosine kinase in said mammal wherein inducing over-expression of said sphingosine kinase level modulates one or more functional characteristics of said endothelial cells.
4. The method according to any one of claims 1-3 wherein said endothelial cell is a vascular endothelial cell.
5. The method according to claim 4 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is one or more of viability, proliferation, differentiation, cell surface molecule expression, cytokine responsiveness or enhanced proliferation or viability.
6. The method according to claim 5 wherein said cell surface molecule is an adhesion molecule.

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7. The method according to claim 5 or 6 wherein said functional characteristic is up-regulated.
8. The method according to claim 4 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is the induction of a pro-inflammatory phenotype.
9. The method according to claim 8 wherein said pro-inflammatory phenotype is down-regulated.
10. The method according to claim 4 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is the induction of an angiogenic phenotype.
11. The method according to claim 10 wherein said angiogenic phenotype is up-regulated.
12. The method according to claim 10 wherein said angiogenic phenotype is down-regulated.
13. The method according to claim 4 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is maintenance of the CD34⁺ endothelial cell progenitor phenotype.
14. The method according to claim 13 wherein said CD34⁺ progenitor phenotype is maintained.
15. The method according to claim 3 wherein said condition is vascular engraftment, wound repair, tissue or organ transplantation or the repair of devascularised tissue and said modulated endothelial cell functional characteristic is one or more of enhanced endothelial cell proliferation, enhanced endothelial cell viability or

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maintenance of the CD34⁺ endothelial cell progenitor phenotype.

16. The method according to claim 3 wherein said condition is an inflammatory condition and said modulated endothelial cell functional characteristic is down-regulation of one or more of an endothelial cell inflammatory or angiogenic phenotype.
17. The method according to claim 16 wherein said condition is rheumatoid arthritis.
18. The method according to claim 3 wherein said condition is characterised by unwanted angiogenesis and said modulated endothelial cell functional characteristic is down-regulation of an endothelial cell angiogenic phenotype.
19. The method according to claim 18 wherein said condition is a tumour.
20. The method according to any one of claims 1-8, 10-11 or 13-15 wherein said modulation is up-regulation of sphingosine kinase levels and said up-regulation is achieved by introducing into said endothelial cell a nucleic acid molecule encoding sphingosine kinase or functional equivalent, derivative or homologue thereof or the sphingosine kinase expression product or functional derivative, homologue, analogue, equivalent or mimetic thereof.
21. The method according to any one of claims 1-19 wherein said modulation is achieved by contacting said endothelial cell with a proteinaceous or non-proteinaceous molecule which modulates transcriptional and/or translational regulation of the sphingosine kinase gene.
22. The method according to any one of claims 1-8, 10-11 or 13-15 wherein said modulation is up-regulation of sphingosine kinase levels and said up-regulation is achieved by contacting said endothelial cell with a proteinaceous or non-proteinaceous molecule which functions as an agonist of the sphingosine kinase

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expression product.

23. The method according to any one of claims 1-6, 8-10, 12-13 or 16-19 wherein said modulation is down-regulation of sphingosine kinase levels and said down-regulation is achieved by contacting said endothelial cell with a proteinaceous or non-proteinaceous molecule which functions as an antagonist to the sphingosine kinase expression product.
24. The method according to claim 23 wherein said molecule is a mutant sphingosine kinase which mutant is characterised by substitution of the glycine residue at position 82 to aspartate.
25. The method according to any one of claims 1 or 2 wherein said endothelial cell activity is modulated *in vivo*.
26. The method according to any one of claims 1 or 2 wherein said endothelial cell activity is modulated *in vitro*.
27. Use of an agent capable of modulating the functional level of sphingosine kinase in the manufacture of a medicament for the modulation of one or more endothelial cell functional characteristics in a mammal wherein inducing over-expression of said sphingosine kinase level modulates one or more of the functional characteristics of said endothelial cells.
28. Use according to claim 27 wherein said agent is a proteinaceous or non-proteinaceous molecule which modulates transcriptional and/or translational regulation of the sphingosine kinase gene, functions as an agonist of sphingosine kinase activity or functions as an antagonist of sphingosine kinase activity.
29. Use of sphingosine kinase or a nucleic acid encoding sphingosine kinase in the manufacture of a medicament for the modulation of one or more endothelial cell

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functional characteristics in a mammal wherein inducing over-expression of said sphingosine kinase level modulates one or more of the functional characteristics of said endothelial cells.

30. Use according to any one of claims 27-29 wherein said endothelial cell is a vascular endothelial cell.
31. Use according to claim 30 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is one or more of viability, proliferation, differentiation, cell surface molecule expression, cytokine responsiveness or enhanced proliferation or viability.
32. Use according to claim 31 wherein said cell surface molecule is an adhesion molecule.
33. Use according to claim 30 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is the induction of a pro-inflammatory phenotype.
34. Use according to claim 30 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is the induction of an angiogenic phenotype.
35. Use according to claim 30 wherein said endothelial cell functional characteristic is up-regulatable by sphingosine kinase over-expression and said characteristic is maintenance of the CD34⁺ endothelial cell progenitor phenotype.
36. Use according to claim 35 wherein said CD34⁺ progenitor phenotype is maintained.
37. Use according to any one of claims 27-36 wherein said medicament is used to treat a condition characterised by aberrant or otherwise unwanted endothelial cell

functioning.

38. Use according to claim 37 wherein said condition is vascular engraftment, wound repair, tissue or organ transplantation or the repair of devascularised tissue and said modulated endothelial cell functional characteristic is one or more of enhanced endothelial cell proliferation, enhanced endothelial cell viability or maintenance of the CD34⁺ endothelial cell progenitor phenotype.
39. Use according to claim 37 wherein said condition is an inflammatory condition and said modulated endothelial cell functional characteristic is down-regulation of one or more of an endothelial cell inflammatory or angiogenic phenotype.
40. Use according to claim 39 wherein said condition is rheumatoid arthritis.
41. Use according to claim 37 wherein said condition is characterised by unwanted angiogenesis and said modulated endothelial cell functional characteristic is down-regulation of an endothelial cell angiogenic phenotype.
42. Use according to claim 41 wherein said condition is a tumour.
43. A pharmaceutical composition comprising modulatory agent and one or more pharmaceutically acceptable carriers and/or diluents when used in the method of any one of claims 1-26.